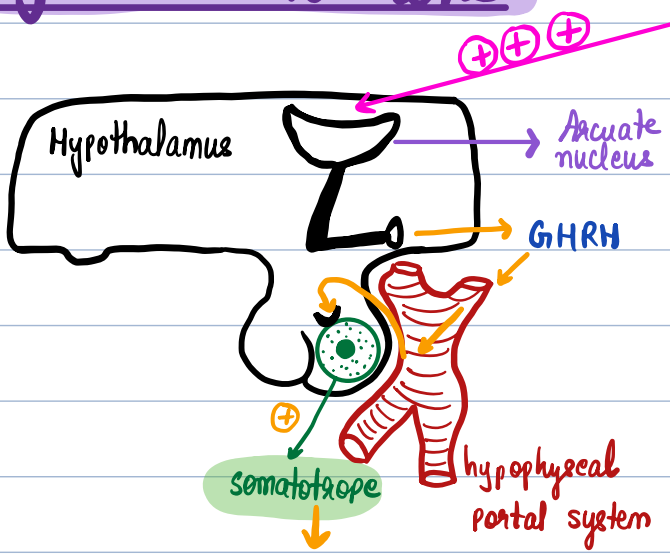
Growth Hormone:



Factors stimulating GHRH release:

- high $\bar{a}.\bar{a}$ in blood
- low glucose level in blood (hypoglycemia)
- low fatty acids in blood
- exercise
- healthy stressors

{STAT = signal transducer activator of transcription}

binds to a tyrosine kinase like receptor in the liver

↓

phosphorylation of JAK

↓

phosphorylation of transcription factor STAT

↓

enters nucleus & binds to a specific gene sequence on DNA

↓

transcription produces mRNA

↓

translation to produce protein IGF-1 (Insulin-like Growth Factor)

↓

IGF-1 enters circulation *

stimulates gluconeogenesis in liver

- GH binds to receptors on adipose cells

↓

activation of hormone sensitive lipase (HSL)

↓

breakdown of triglycerides into glycerol & fatty acids (LIPOLYSIS)

↓

glycerol is used for gluconeogenesis in liver

* IGF - 1

comes out of bloodstream & binds to receptors on skeletal muscle cells

↓

activation of specific signalling pathways

↓

transcription, translation

↓

proteins produced

↓

activation of channels on skeletal muscle cells

↓

uptake of $\bar{a}\cdot\bar{a}$ into cell

↓

formation of proteins from these $\bar{a}\cdot\bar{a}$

↓

increase in muscle size & muscle function

IGF-1 binds to receptors on osteoblast & osteoclast cells of bone

↓

↑ osteoblastic activity
↑ osteoclastic activity
↑ endochondral ossification
↑ collagen type I synthesis

↓

↑ bone mass, density & thickness

IGF - 1 acts on the Chondrocytes present in epiphyseal plate of bone

↓

↑ differentiation
↑ size
↑ proliferation

↓

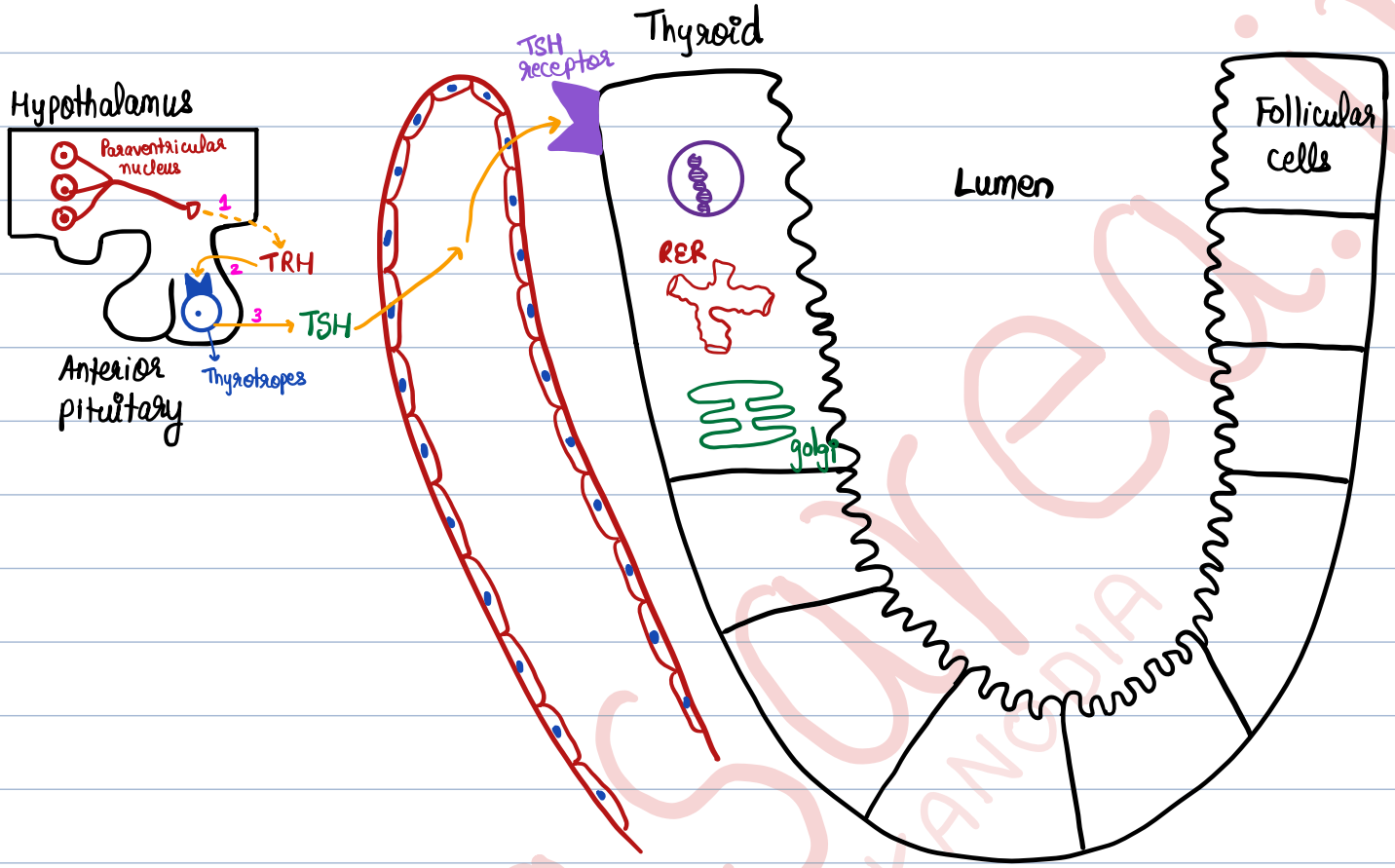
↑ interstitial growth

↓

↑ in length of bone

Thyroid Hormone:

{TRH = Thyrotropin releasing hormone
TSH = Thyroid stimulating hormone}



TSH binds to TSH receptor on follicular cells

↓

activation of G_s protein
(detaching of G_s from GDP & binding to GTP)

↓

activation of adenylate cyclase

ATP → cAMP

↓

activation of protein kinase A

↓

phosphorylation of transcription factor

↓

transcription produces mRNA

↓

mRNA bind to rough ER & undergo translation to produce proteins

↓

proteins are modified & packaged in golgi apparatus

↓

release of protein packed in a vesicle

↓

vesicle fuses with cell membrane of follicular cell

↓

protein is released into lumen → *

↑ iodide (I^-) in bloodstream
([I] iodine ↓ in bloodstream & ↑ in follicular cells)

↓

Iodide (I^-) from blood moves into follicular cell by Na^+ - I^- symporter

↓

pendrin protein pumps I^- from follicular cell into lumen

↓ Iodide oxidation

(TPO) Thyroid peroxidase converts iodide to iodine (I_2)

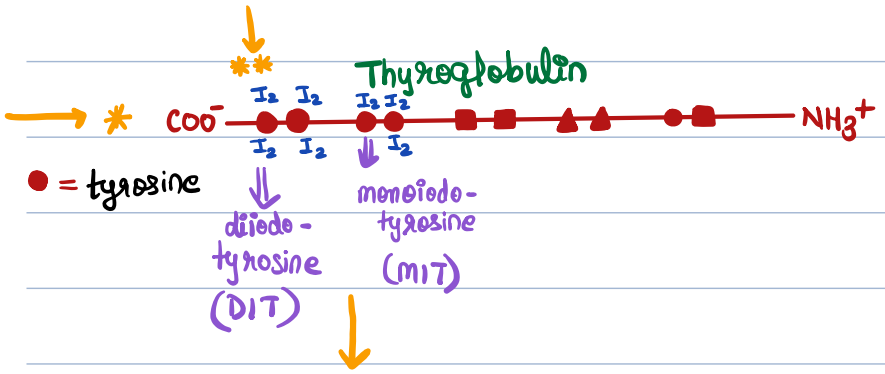
↓

TPO takes I_2 molecules & attaches them to tyrosine residues on thyroglobulin

↓ Iodination

**

Thyroglobulin (TG)



catalysed by TPO

- DIT + DIT ⇒ T_4 (Thyroxine / Tetraiodothyronine)
- MIT + DIT ⇒ T_3 (Triiodothyronine)

T_4 & T_3 are formed on the thyroglobulin molecule

↓ Endocytosis

this complex is endocytosed into the follicular cell & packed into a vesicle

↓

lysosomes fuse with the vesicle

↓

lysosomal enzymes cut the thyroglobulin colloid to isolate T_3 & T_4 molecules

↓

the vesicle now fuses with cell membrane of follicular cells

↓

isolated T_3 & T_4 are released into bloodstream

↓

∵ T_3 & T_4 are not water soluble ∴ they are transported by a protein in bloodstream called <u>Thyroxine-binding Globulin</u> (synthesized in liver)

- $T_4 > T_3$ (in blood)
- T_4 has the ability to pass through lipid bilayers & enter cells

T_4 enters the target cell

↓

5'- deiodinase removes an iodine residue from T_4

T_4 → T_3 (active)

↓

T_3 binds to transcription factor along with retinoic acid

↓

transcription factor is activated

↓

activated transcription factor stimulates a particular gene sequence in nucleus

↓

proteins are produced

↓

these proteins get inserted in cell membrane

↓

proteins act as Na^+- K^+ ATPase pumps

↓

decrease in cellular ATP levels

↓

increased oxidation of glucose to produce more ATP

(O_2 usage ↑)

↑ metabolic rate (BMR)

- ↑ number & size of mitochondria to ↑ ATP production
- ↑ heat production

Effects on Liver:

→ stimulates glycogenolysis

→ stimulates gluconeogenesis

→ increase the number of LDL receptors in liver (↑ LDL uptake by liver)

Effects on heart:

→ increases β_1 adrenergic receptors in myocytes → ↑ contractily → ↑ stroke volume → ↑ cardiac output → ↑ BP

→ increases β_1 adrenergic receptors in nodal cells → ↑ HR

Effects on CNS:

→ ↑ dendrite formation in neurons

→ ↑ myelination of axons

→ ↑ in number of synapses

Effects on Bone:

→ maintains balance between osteoblastic & osteoclastic activity

→ stimulates interstitial growth (↑ in length of epiphyseal plates)

→ stimulating endochondral ossification

→ helps in bone remodelling

Effect on Adipose Tissue:

→ ↑ lipolysis

Effect on Muscles:

→ maintains balance between protein anabolism & catabolism (in hyperthyroidism, there is excess protein catabolism)

Effect on Skin:

→ ↑ sweat production (↑ evaporative cooling)

→ ↑ cutaneous vasodilation ↓ ↑ redness of skin

Effect on GIT:

→ ↑ secretions of GI tract

→ ↑ contractility of smooth muscles → ↑ motility of GI tract

Oxytocin: produced by paraventricular nucleus in hypothalamus & secreted by posterior pituitary.

→ dilatation of cervix activates stretch receptors → stimulates the posterior pituitary to secrete oxytocin

oxytocin binds to oxytocin receptor on smooth muscle cell of myometrium

↓

activation of G_q protein

↓

activation of membrane phospholipase - C

↓

phospholipase C breaks down PIP_2 in cell membrane into DAG, IP_3

- IP_3 stimulates the caveolae to push in Ca^{2+} into the cell → ↑ intracellular Ca^{2+}
- DAG activates protein kinase - C → phosphorylation of cell membrane proteins to ↑ Ca^{2+} influx

↓

↑ contraction

↓

↑ expulsion of fetus

Suckling of infant

↓

activation of mechanoreceptors on nipple

↓

hypothalamus releases oxytocin

↓

oxytocin acts on myoepithelial cells of mammary gland

↓

activation of G_q protein

↓

activation of membrane phospholipase - C

↓

phospholipase C breaks down PIP_2 in cell membrane into DAG and IP_3

- IP_3 stimulates the caveolae to push in Ca^{2+} into the cell

↓

↑ intracellular Ca^{2+}

- DAG activates protein kinase - C

↓

phosphorylation of cell membrane proteins to ↑ Ca^{2+} influx

↓

↑ contraction

↓

↑ milk ejection (milk let-down reflex)

Hypersecretion of Oxytocin: (rare)

→ ptosin (synthetic oxytocin) to aid in birthing

Hyposecretion of Oxytocin:

→ uterine inertia

Insulin: secreted by β-cells in islets of Langerhans of Pancreas.

→ stimulus for insulin synthesis & secretion: hyperglycemia

→ insulin is synthesized as pre-proinsulin (has an extra attached C-peptide)

hyperglycemia

↓

glucose moves into β-cell by GLUT-2 (insulin independent)

↓

glucose undergoes glycolysis & Kreb's Cycle to produce NADHs & FADHs

↓

oxidative phosphorylation produces ATP

↓

ATP binds to K^+ channel & closes it preventing K^+ efflux

↓

accumulation of +ve charge in cell

↓

increase in membrane potential

↓

stimulation of Ca^{2+} channels causing Ca^{2+} influx

↓

Ca^{2+} causes linking of synaptoproteins between the insulin vesicle & cell membrane causing them to fuse

↓

insulin (along with C-peptide & amylin) is released into blood

∴ C-peptide in blood is a marker for insulin levels in blood.

Insulin binds to tyrosine Kinase receptor on liver

↓

phosphorylation of tyrosine residues

↓

activation of PI_3K & AKT proteins

↓

glucose is brought into the liver by GLUT-2

↓

- PI_3K/AKT polymerizes glucose into glycogen (glycogenesis)
- PI_3K/AKT also converts glucose to pyruvate → acetyl coA → ATP production (glycolysis)

- GLUT-2 is insulin-independent
- GLUT-4 is insulin-dependent

Insulin binds to tyrosine Kinase receptor in muscle cell

↓

phosphorylation of tyrosine residues

↓

activation of PI_3K & AKT proteins

↓

activation of GLUT-4

↓

↑ glucose uptake into muscle cell

↓

insulin in muscle cell stimulates glycolysis & glycogenesis

activates amino acid channels

↓

↑ uptake of amino acids into muscle

↓

↑ protein synthesis

Insulin binds to tyrosine kinase receptors on adipose cells

↓

phosphorylation of tyrosine residues

↓

activation of PI_3K & AKT proteins

↓

activation of GLUT-4

↓

↑ glucose uptake into muscle cell

↓

stimulation of Krebs' cycle

↓

PI_3K / AKT stimulate conversion of DHAP to glycerol & conversion of acetyl CoA into fatty acids

↓

glycerol combines with fatty acids to form triglycerides (TAG)

[Lipogenesis ↑]